AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listing, of claims in the application.

Listing of Claims

1. (Withdrawn) A chemical conjugate between an immunoglobulin Fab fragment and molecular entities imparting diagnostic or therapeutic utility, whereby the only sites of conjugation on the Fab fragment are one or both of the sulfhydryl groups deriving from the selective and quantitative reduction of the inter-chain disulfide bond of said Fab fragment and whereby said molecular entities imparting diagnostic or therapeutic utility have at least one free sulfhydryl-reactive group, characterized in that the conjugation stoichiometric molar ratio of molecular entity to Fab fragment is in the range from 0.95 to 1.05 or in the range from 1.95 to 2.05.

2. (Withdrawn) A conjugate according to claim 1, wherein the first of said sulfhydryl groups deriving from the selective and quantitative reduction of the inter-chain disulfide bond is quantitatively functionalized by reaction with one of said molecular entities imparting diagnostic or therapeutic utility.

3. (Withdrawn) A conjugate according to claim 2, wherein the second of said sulfhydryl groups deriving from the selective and quantitative reduction of the inter-chain disulfide bond is quantitatively functionalized by reaction with a second of said molecular entities imparting diagnostic or therapeutic utility, said second molecular entity being different or identical to the first one.

4. (Withdrawn) A conjugate according to claim 1, wherein both of said sulfhydryl groups deriving from the selective and quantitative reduction of the inter-chain disulfide bond are quantitatively symmetrically functionalized by reaction with a stoichiometric excess of one of said molecular entities imparting diagnostic or therapeutic utility.

5. (Withdrawn) A conjugate according to claim 1, wherein one of said sulfhydryl groups deriving from the selective and quantitative reduction of the inter-chain disulfide bond is

chemically modified by reaction with a chemical moiety non-imparting diagnostic or therapeutic utility, said chemical moiety being preferably selected from the group consisting of protective groups of the thiol groups small alkylating and arylating agents.

6. (Withdrawn) A conjugate according to claim1, wherein said molecular entities imparting diagnostic or therapeutic utility comprise derivatives of chelating agents for, or chelates of, radionuclides, paramagnetic metal ions or luminescent metal ions, a chromophoric fluorescent or a phosphorescent molecule, a biotin molecule, a hapten recognized by a distinct antibody or fragment thereof, an avidin or streptavidin molecule, a therapeutic drug, a lipophilic chain bearing molecular entity incorporated into liposomes, phospholipid-stabilized microbubbles, triglyceride- or polymer-based microspheres, microballoons which carry the diagnostic or therapeutic agent.

7. (Withdrawn) A conjugate according to claim 6, wherein said molecular entities further comprise one or more functional groups which may be used, as such or after deprotection or after chemical modification, as targets for the selective attachment of a second Fab fragment, equal or different from the first one, or of a second molecular entity imparting diagnostic or therapeutic utility.

8. (Withdrawn) A conjugate according to any one of claims 1 to 6, wherein said sulfhydryl reactive groups comprise iodoacetyl, bromoacetyl, vinyl, maleimido groups or polyfluorobenzene or dinitrofluorobenzene derivatives.

9. (Withdrawn) A conjugate according to any one of claims 1 to 7, wherein the Fab fragment is a recombinant Fab.

10. (Currently amended) A process for the preparation of a chemical conjugate between an immunoglobulin Fab fragment and molecular entities imparting diagnostic utility, whereby the only sites of conjugation on the Fab fragment are one or both of the sulfhydryl groups deriving from the selective and quantitative reduction of the inter-chain disulfide bond of said Fab fragment and whereby said molecular entities imparting diagnostic utility have at least one free

sulfhydryl-reactive group, characterized in that the conjugation stoichiometric molar ratio of molecular entity to Fab fragment is in the range from 0.95 to 1.05 or in the range from 1.95 to 2.05 ~~the conjugate of claim1~~, comprising:

a) the selective and quantitative reduction of the inter-chain disulfide bond of a Fab fragment to give two free sulfhydryl groups using TCEP in a concentration of 0.1 – 10 mM; and

b) the quantitative functionalization of one or both of the sulfhydryl groups from step a) with molecular entities having at least one free sulfhydryl-reactive group and imparting diagnostic ~~or therapeutic~~ utility, to give mono- or diconjugate compounds, said diconjugates deriving from either symmetric or asymmetric functionalization of the sulfhydryl groups.

11 - 12 (cancelled).

13. (Currently amended) The process of claim ~~11~~ 10, wherein the reduction is carried out mixing the reacting species under buffered conditions giving a final buffered aqueous reaction solution having the following characteristics:

Fab concentration	:	1 – 100 μM;
~~Phosphine concentration~~	:	~~0.1 – 10 mM;~~
pH of the buffered solution	:	4 – 8;
reaction time	:	5 – 180 min;
reaction temperature	:	4 – 45 °C.

14. (Currently amended) The process of claim 13, wherein the conditions are the following:

Fab concentration	:	1.5 – 10 μM or 1 – 5 μM;
~~Phosphine~~ TCEP concentration	:	0.5 – 5 mM;
pH of the buffered solution	:	5 – 7;
reaction time	:	25 – 70 min;
reaction temperature	:	25 – 40 °C.

15. (Original) The process of claim 10, wherein said quantitative functionalization of step b) is performed immediately at the end of the reduction step a), in the same reaction

medium, by adding a buffered aqueous solution of the conjugating molecular entity, without purifying the reduced Fab fragment.

16. (Currently amended) The process of claim 15, wherein the final buffered aqueous reaction solution has the following characteristics:

Fab concentration	:	2 – 5 μM;
~~Phosphine~~ TCEP concentration	:	0.5 – 5 mM;
conjugating moiety concentration	:	0.1 – 100 mM;
pH of the buffered solution	:	5 – 7;
reaction time	:	≥ 30 min;
reaction temperature	:	4 – 45 °C or 20 – 40 °C.

17. (Withdrawn) N^2,N^2-bis[2-[bis(carboxymethyl)amino]ethyl]-N^6-[4-(2,5-dioxo-1*H*-pyrrol-1-yl)-1-oxobutyl]-L-lysine as intermediate compound for the preparation of conjugates of claim 1.

18. (Withdrawn) Pharmaceutical compositions containing as active ingredients the conjugate compounds of claim 1.

19. (Withdrawn) Compositions according to claim 18, wherein said conjugate compounds are formulated in the form of suspensions, solutions, emulsions for parenteral administration, lyophilizates to be reconstituted before use.

20. (Withdrawn) Compositions according to claim 18, wherein the dose of the active ingredient ranges from 0.1 to 10 mg of conjugate per single administration.

21. (Withdrawn) Compositions according to claim 18, wherein the dose of the active ingredient ranges from 10 to 500 mg of conjugate per single administration.

22. (Withdrawn) Compositions according to claim 18, for use in analytical immunochemical tests *in vitro*.